Synthesis of Sugar Azido or Amino Esters and Their Use as Building Blocks for the Preparation of Saccharide Nucleosides

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Several sugar azido or amino esters bearing an α- or a β-*C*-D-glucopyranosyl backbone have been prepared by TMSOTf/Ac_2O-mediated α-*C*-glycosylation with concurrent selective removal of the primary benzyl group or selective acetolysis of the primary benzyl group of β-*C*-glycoside as key steps. Such structures have been successfully used as scaffolds for the synthesis of novel saccharide nucleosides.

Introduction

Recent advances in carbohydrates and glycobiology have revealed many important functions of saccharides in biological systems.[1] Within cells, carbohydrate modifications are essential to modulate the structure and functions of proteins and lipids. In the extracellular milieu, they are associated with cellular recognition in infection, cancer, and immune response. It is also known that some carbohydrate-based drugs aimed at fighting inflammation, cancer, and viruses are currently in clinical trials.[2] For these reasons, the design and synthesis of novel carbohydrates are of particular importance for biological studies.[1d,3] Combinatorial methodology occupies a promising position in this area of research because of its ability to generate large numbers of structurally diverse molecules. In this regard, though, it is necessary to develop new building blocks for provision of useful combinatory molecular diversity.

Sugar amino acids (SAAs) are recently developed carbohydrate derivatives bearing both amino and carboxylic groups on furan or pyran backbones.[4] Thanks to their amino and carboxylic acid functions, SAAs have been used as scaffolds in the design and synthesis of peptidomimetics,[5] enzyme inhibitors,[6] cyclic sugar amino acid/amino acid hybrid molecules,[7] oligomers,[8] and polymers.[9] Since the D-glucopyranoside unit is a fundamental constituent of glycoconjugates and *C*-glycosidic analogues of natural carbohydrate derivatives are good mimics resistant to glycosidase-catalyzed hydrolysis,[10] we decided to investigate SAAs bearing α- or β-*C*-D-glucopyranosyl frameworks and their use as building blocks for the preparation of novel saccharide nucleosides. Saccharide nucleosides are an important class of natural nucleoside antibiotics.[11] Furthermore, several natural SAAs have been found in nucleoside antibiotics, such as ezomycin A,[11] gougerotin,[12] and aspiculamycin.[13] However, no synthetic SAA-based saccharide nucleoside has ever been reported. The polyfunctionality of SAAs should allow the creation of diverse saccharide nucleoside libraries. These saccharide nucleosides may be potential inhibitors of glycosyltransferases or drug candidates, since they would not be recognized by carbohydrate-processing enzymes. Here we report an easy synthesis of four sugar azido or amino esters (**1**−**4**; Figure 1) and the preparation of several novel saccharide nucleosides with SAAs as scaffolds.

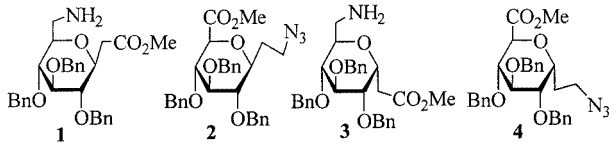

Figure 1. Structures of sugar azido or amino esters **1**−**4**

Results and Discussion

The preparation of compounds **1**−**4** was designed to maximize efficiency by derivation from common starting materials. Azido or amino esters **1** and **2** were obtained from the readily available tetra-*O*-benzyl-β-*C*-D-glucoside **5**.[14] As shown in Scheme 1, a one-pot, TMSOTf/Ac_2O-mediated debenzylation/acetylation of the 6-benzyloxy group[15] in **5** afforded the key intermediate **6** after deacetylation under Zemplén conditions. The alcohol **6** was transformed into azide **7** by displacement of the mesylate. The alkene function was oxidized to a carboxylic acid by a combination of OsO_4 and Jones reagent.[16] The corresponding methyl ester was obtained in 75% yield over two

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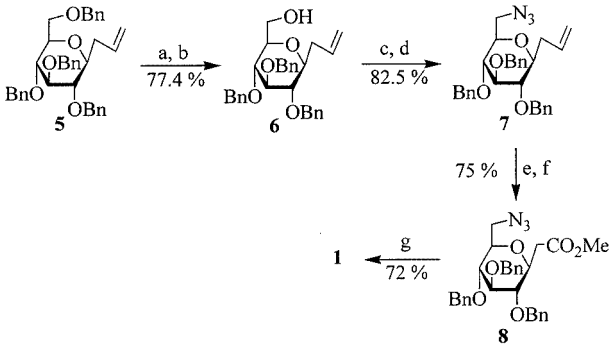
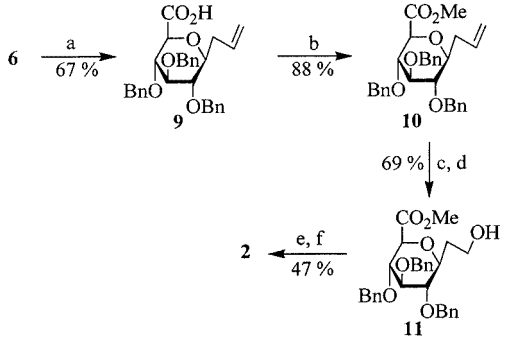
steps. Finally, the azide was reduced to amine **1** by a Staudinger reaction.

The synthesis of the azido ester **2** is outlined in Scheme 2. Oxidation of the primary alcohol function of **6** with TEMPO/NaOCl[17] and subsequent esterification furnished ester **10**. Oxidative cleavage (OsO_4/$NaIO_4$) of the double bond, followed by reduction ($NaBH_4$), afforded the alcohol **11** in 69% yield. As before, the azide was introduced via the mesylate to give compound **2**.

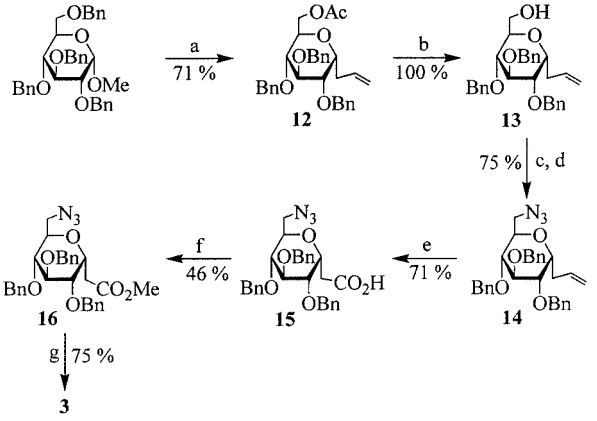
SAA derivatives **3** and **4** containing an α-C-glycosidic linkage can be prepared from the known 6-deprotected α-*C*-allyl glucoside **13**.[8c] This has in turn been obtained in 27% overall yield from 1,6-β-D-anhydroglucose in a two-



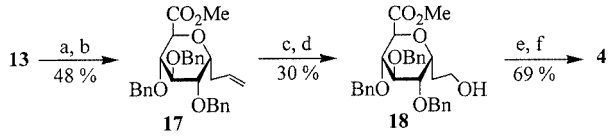
Scheme 1. Synthesis of sugar amino ester **1**; reagents and conditions: (a) Ac_2O, TMSOTf, CH_2Cl_2, −40 °C, Ar; (b) MeONa, MeOH, room temp.; (c) MsCl, TEA, CH_2Cl_2, 0 °C to room temp.; (d) NaN_3, DMF, 90 °C; (e) OsO_4, Jones reagent, acetone, room temp.; (f) MeI, $NaHCO_3$, DMF, room temp.; (g) PPh_3, H_2O, THF, room temp.



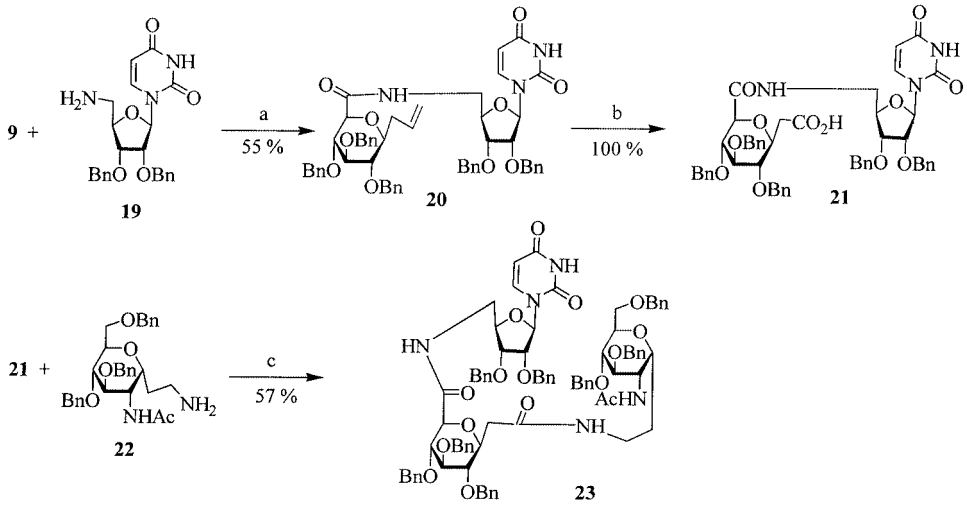
Scheme 2. Synthesis of sugar azido ester **2**; reagents and conditions: (a) TEMPO, KBr, NaOCl, $NaHCO_3$, room temp.; (b) MeI, $NaHCO_3$, DMF, room temp.; (c) OsO_4, $NaIO_4$, THF, H_2O, room temp.; (d) $NaBH_4$, MeOH, room temp.; (e) MsCl, TEA, CH_2Cl_2, 0 °C to room temp.; (f) NaN_3, DMF, 90 °C



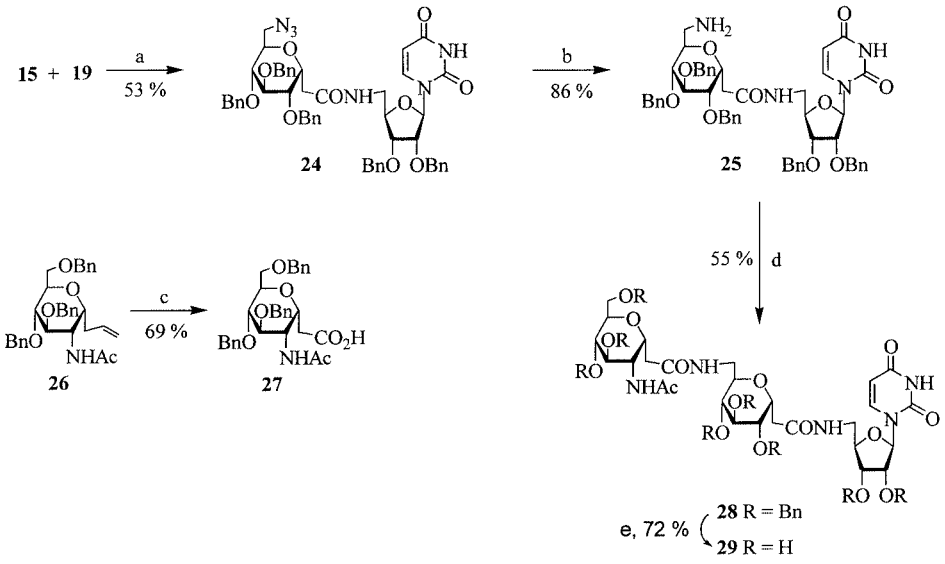
Scheme 3. Synthesis of sugar amino ester **3**; reagents and conditions: (a) AllylTMS, TMSOTf, CH_2Cl_2, 0 °C, Ar, then Ac_2O; (b) MeONa, MeOH, room temp.; (c) MsCl, TEA, CH_2Cl_2, 0 °C to room temp.; (d) NaN_3, DMF, 90 °C; (e) $KMnO_4$, Aliquat 336, H_2O, AcOH, CH_2Cl_2, room temp.; (f) MeI, $NaHCO_3$, DMF, room temp.; (g) PPh_3, H_2O, THF, room temp.



Scheme 4. Synthesis of sugar azido ester **4**; reagents and conditions: (a) Jones reagent, acetone, room temp.; (b) MeI, $NaHCO_3$, DMF, room temp.; (c) OsO_4, $NaIO_4$, THF, H_2O, room temp.; (d) $NaBH_4$, MeOH, room temp.; (e) MsCl, TEA, CH_2Cl_2, 0 °C to room temp.; (f) NaN_3, DMF, 90 °C



Scheme 5. Synthesis of disaccharide nucleoside **23**; reagents and conditions: (a) IIDQ, CH_2Cl_2, room temp.; (b) OsO_4, Jones reagent, acetone, room temp.; (c) *i*BuOCOCl, TEA, CH_2Cl_2, −10 °C to room temp.



Scheme 6. Synthesis of disaccharide nucleoside **29**; reagents and conditions: (a) DIPC, HOBt, THF, CH_2Cl_2, 0 °C to room temp.; (b) PPh_3, H_2O, THF, room temp.; (c) OsO_4, Jones reagent, acetone, room temp.; (d) **27**, *i*BuOCOCl, TEA, CH_2Cl_2, −10 °C to room temp.; (e) Pd/C 10%, MeOH, room temp.

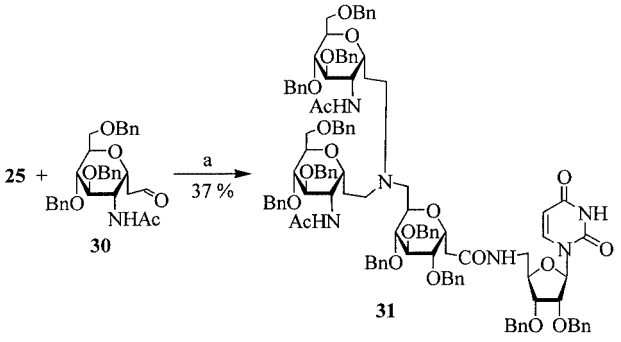
step reaction sequence. We used an alternative approach, with the less expensive methyl tetra-*O*-benzyl-α-D-glucopyranoside as starting material (Scheme 3). The 6-*O*-acetyl-α-*C*-allyl glucoside **12** was prepared first, in 71% yield, with allyl trimethylsilane in the presence of TMSOTf, followed by addition of Ac_2O, in a procedure reported by Hung et al.[18] Subsequent deacetylation quantitatively furnished the alcohol **13**. The known compounds **14** to **16** were synthesized as described.[8c] Final reduction of the azide **16** afforded amino ester **3** in 75% yield. The azido ester **4** was generated in a similar way to compound **2** (Scheme 4).

With these SAA derivatives in hand, we then investigated the feasibility of linking these molecules with nucleoside and other sugar derivatives to construct novel saccharide nucleosides. As shown in Scheme 5, coupling of the acid **9** with the nucleoside **19**[19] in the presence of IIDQ (2-isobutoxy-1-isobutoxycarbonyl-1,2-dihydroquinoline) provided the saccharide nucleoside **20** in 55% yield. Oxidation and further condensation with the amino group of the *C*-glycoside **22**[20] by the mixed anhydride method gave the disaccharide nucleoside **23** in 57% yield.

Treatment of the azido acid **15** with the nucleoside **19**, catalyzed by 1,3-diisopropylcarbodiimide (DIPC)/*N*-hydroxybenzotriazole (HOBt), resulted in saccharide nucleoside **24**, which was reduced to the amine **25** with PPh_3 (Scheme 6). Oxidation of the amino *C*-allyl glucoside **26**[19] with OsO_4/Jones reagent afforded the acid **27**. Condensation of this with the amine **25** provided another disaccharide nucleoside **28**. Hydrogenolysis of **28** with Pd/C in MeOH gave the fully deprotected compound **29** in 72% yield. Alternatively, reductive amination of **25** with 2 equiv. of aldehyde **30**[19] in the presence of $NaBH_3CN/ZnCl_2$[21] yielded the trisaccharide nucleoside **31** in 37% yield (Scheme 7).

Conclusions

D-Glucose-derived α- or β-*C*-glycosyl sugar azido or amino esters have been conveniently synthesized by TMSOTf/Ac_2O-mediated α-*C*-glycosylation with concurrent selective removal of the primary benzyl group or selective acetolysis of the primary benzyl group of β-*C*-glycoside as key steps. Our method should be applicable to the synthesis of other SAA derivatives with amino and carboxylic acid functions on the hexose 1- and 6-positions, since the key intermediate allyl 6-deprotected α- and β-*C*-glycosides are easily accessible.[14,15,18] Allenyl or vinyl *C*-glycosides could be processed in a similar way to generate homologous compounds.[18,22] Several saccharide nucleosides, bearing mono-, di-, or trisaccharide units, have been successfully prepared by use of SAAs as carbohydrate scaffolds. Compounds such as **29** could be potential inhibitors of *N*-acetylglycoaminyltransferases, as a monosaccharide has been used as the Mn^{2+}−pyrophosphate complex mimic of the donor sub-



Scheme 7. Synthesis of trisaccharide nucleoside **31**; reagents and conditions: (a) $ZnCl_2$, $NaBH_3CN$, MeOH, room temp.

strate.[23] Modification of the sugar backbone and further improvements in design would be expected to result in novel molecular frameworks that may exhibit interesting biological properties. Furthermore, compounds possessing a 6-methoxycarbonyl group as shown in Schemes 2 and 4 should also be useful building blocks for the synthesis of glucuronate derivatives.[24]

Experimental Section

General Methods: Melting points were measured with a Thomas-Hoover apparatus. ^1H and ^{13}C NMR spectra were recorded with a Bruker AGH 250 spectrometer in $CDCl_3$ solutions. Assignments were aided by $^1H/^1H$ and $^1H/^{13}C$ correlations, and the Dept 135 technique. Optical rotations were measured with a Perkin−Elmer 141 polarimeter in a 10-cm 1-mL cell. Column chromatography was performed on E. Merck 60 silica gel (230−400 mesh). Analytical thin layer chromatography was performed on E. Merck aluminum percolated plates of 60F-254 silica gel with detection by UV and by spraying with 6 N H_2SO_4 and then heating for about 2 min at 300 °C. THF was distilled from sodium and benzophenone prior to use. Dichloromethane was distilled from P_2O_5. Microanalyses were performed at the Service de Microanalyse de l'Université Pierre et Marie Curie. Fast atom bombardment mass spectra (FAB-MS) were recorded with a JMS-700 spectrometer at the Service de Spectromètrie de Masse de l'Ecole Normale Supérieure de Paris. Infrared spectra were recorded with a UNICAM Mattson 1000 FTIR spectrometer.

3-(2′,3′,4′-Tri-*O*-benzyl-β-D-glucopyranosyl)-1-propene (6): A solution of TMSOTf (144 μL, 0.8 mmol) in CH_2Cl_2 (1.5 mL) was added at −40 °C under argon to a solution of 3-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-glucopyranosyl)-1-propene[14] (2.256 g, 4.000 mmol) in anhydrous CH_2Cl_2 (16 mL) and Ac_2O (16 mL). After 1 h, the reaction was quenched with saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (2× 50 mL), the combined organic layers were washed with water, dried with $MgSO_4$, and filtered, and the solvents were evaporated. The crude 3-(6′-*O*-acetyl-2′,3′,4′-tri-*O*-benzyl-β-D-glucopyranosyl)-1-propene was then dissolved in MeOH (30 mL) and treated with MeONa (1 M, 1 mL). After 20 h at room temp., the reaction mixture was neutralized with 10% HCl at 0 °C and MeOH was removed under vacuo. The resulting residue was extracted with EtOAc (2× 50 mL) and washed with brine. The combined organic layers were dried with $MgSO_4$ and filtered, and the solvents were evaporated. Purification by column chromatography (Et_2O/hexane, 1:1) yielded **6** as a white solid (1.467 g, 77.4%). R_f = 0.21 (Et_2O/hexane, 1:1). M.p. 62 °C. $[\alpha]_D$ = +10 (c = 0.8, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3397 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.81 (t, $J_{OH,6'a}$ = $J_{OH,6'b}$ = 6.5 Hz, 1 H, OH), 2.20−2.38 (m, 1 H, 3-H_a), 2.57−2.68 (m, 1 H, 3-H_b), 3.32−3.42 (m, 3 H, 1′-H, 2′-H, 5′-H), 3.54 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.3 Hz, 1 H, 4′-H), 3.85 (ddd, $J_{5',6'a}$ = 2.8, ^2J = 11.8, $J_{OH,6'a}$ = 6.5 Hz, 1 H, 6′-H_a), 3.60−3.68 (m, 1 H, 6′-H_b), 3.75 (t, $J_{2',3'}$ = $J_{3',4'}$ = 8.8 Hz, 1 H, 3′-H), 4.66 (d, ^2J = 10.8 Hz, 1 H, CH-Ph), 4.67 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.82−4.99 (m, 4 H, 4× CH-Ph), 5.07−5.14 (m, 2 H, 1-H), 5.80−5.98 (m, 1 H, 2-H), 7.21−7.31 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 36.4 (C-3), 62.7 (C-6′), 75.5, 75.6, 76.0 (OCH_2), 78.8, 78.9, 79.4, 82.0 (C-1′,2′,4′,5′), 87.5 (C-3′), 117.8 (C-1), 128.2, 128.3, 128.5, 129.0 (CH-Ph), 134.9 (C-2), 138.4, 138.6, 139.0 (C-*ipso*) ppm. $C_{30}H_{34}O_5$ (474.6): calcd. C 75.92, H 7.22; found C 75.80, H 7.17.

3-(6′-Azido-2′,3′,4′-tri-*O*-benzyl-6′-deoxy-β-D-glucopyranosyl)-1-propene (7): Methanesulfonyl chloride (74 μL, 0.957 mmol) was added at 0 °C to a solution of the alcohol **6** (316 mg, 0.666 mmol) and TEA (170 μL, 1.227 mmol) in CH_2Cl_2 (2 mL). The ice bath was removed, and stirring was continued for 18 h, after which MeOH (50 μL) was added. The solution was concentrated, and the residue was dissolved in EtOAc (20 mL), and washed successively with water, $NaHCO_3$ (5%), and brine. The organic layer was dried with $MgSO_4$, filtered, and concentrated to an oil, which was used directly without purification. This mesylate was dissolved in DMF (2 mL) and added to NaN_3 (216 mg, 3.330 mmol). The reaction mixture was heated at 90 °C for 20 h. After concentration, the residue was diluted in EtOAc (20 mL), washed successively with water and brine, dried with $MgSO_4$, filtered, and concentrated to an oil, which was purified by flash chromatography (EtOAc/cyclohexane, 1:4) to afford **7** as a white solid (274 mg, 82.5%). R_f = 0.68 (EtOAc/cyclohexane, 1:3). M.p. 50 °C. $[\alpha]_D$ = +37 (c = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 2119 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.18−2.24 (m, 1 H, 3-H_a), 2.47−2.56 (m, 1 H, 3-H_b), 3.17 (dd, ^2J = 12.8, $J_{5',6'b}$ = 4.8 Hz, 1 H, 6′-H_b), 3.24−3.46 (m, 5 H, 1′-H, 2′-H, 4′-H, 5′-H, 6′-H_a), 3.62 (t, $J_{2',3'}$ = $J_{3',4'}$ = 8.0 Hz, 1 H, 3′-H), 4.52 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.59 (d, ^2J = 10.8 Hz, 1 H, CH-Ph), 4.76−4.84 (m, 4 H, 4× CH-Ph), 4.99−5.05 (m, 2 H, 1-H), 5.78−5.92 (m, 1 H, 2-H), 7.15−7.27 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 36.4 (C-3), 51.8 (C-6′), 75.7, 76.1 (OCH_2), 78.8, 79.2, 79.5, 81.9 (C-1′,2′,4′,5′), 87.5 (C-3′), 118.0 (C-1), 128.2, 128.4, 128.5, 129.0 (CH-Ph), 134.6 (C-2), 138.3, 138.6, 138.9 (C-*ipso*) ppm. $C_{30}H_{33}N_3O_4$ (499.6): calcd. C 72.12, H 6.66, N 8.41; found C 72.33, H 6.77, N 8.24.

Methyl (6′-Azido-2′,3′,4′-tri-*O*-benzyl-6′-deoxy-β-D-glucopyranosyl)ethanoate (8): A 4 wt% solution of OsO_4 in *t*BuOH (35 μL) and Jones reagent (1 M, 0.35 mL, 0.350 mmol) were added to a solution of **7** (50 mg, 0.100 mmol) in acetone (1 mL). After stirring for 20 h at room temp., the mixture was concentrated, and the residue was dissolved in EtOAc (10 mL) and washed successively with water and brine. The organic layer was dried with $MgSO_4$, filtered, and concentrated to an oil, which was dissolved in DMF (0.5 mL). Sodium bicarbonate (20 mg, 0.238 mmol) was added to the solution, followed by methyl iodide (20 μL, 0.318 mmol). After 20 h, the mixture was concentrated and then diluted in EtOAc. The organic solution was washed successively with water and brine, dried with $MgSO_4$, filtered, and concentrated to an oil, which was purified by preparative layer chromatography (EtOAc/cyclohexane, 1:3) to afford **8** as a white solid (40 mg, 75%). R_f = 0.36 (Et_2O/hexane, 1:2). M.p. 69 °C. $[\alpha]_D$ = +15 (c = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 2119, 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.38 (dd, ^2J = 15.3, $J_{2a,1'}$ = 8.3 Hz, 1 H, 2-H_a), 2.70 (dd, ^2J = 15.3, $J_{2b,1'}$ = 3.8 Hz, 1 H, 2-H_b), 3.16−3.23 (m, 1 H, 6′-H), 3.30−3.47 (m, 4 H), 3.58 (s, 3 H, OMe), 3.65−3.79 (m, 2 H), 4.54 (d, ^2J = 11.3 Hz, 1 H, CH-Ph), 4.60 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.81−4.90 (m, 4 H, 4× CH-Ph), 7.10−7.31 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 37.7 (C-2), 51.6 (C-6′), 52.2 (Me), 75.6, 76.0 (OCH_2), 76.3, 79.0, 79.3, 81.6, 87.3 (C-1′,2′,3′,4′,5′), 128.1, 128.2, 128.3, 128.4, 128.9 (CH-Ph), 138.1, 138.2, 138.7 (C-*ipso*), 171.6 (CO) ppm. $C_{30}H_{33}N_3O_6$ (531.6): calcd. C 67.78, H 6.26, N 7.90; found C 67.46, H 6.40, N 7.80.

Methyl (6′-Amino-2′,3′,4′-tri-*O*-benzyl-6′-deoxy-β-D-glucopyranosyl)ethanoate (1): Ph_3P (22 mg, 0.083 mmol) and water (15 μL, 0.833 mmol) were added to a solution of **8** (40 mg, 0.075 mmol) in THF (1 mL). The mixture was stirred at room temp. for 20 h. After concentration, the residue was purified by preparative layer chromatography (MeOH/CH_2Cl_2, 1:13) to afford **1** as a white solid (28 mg, 72%). R_f = 0.52 (MeOH/CH_2Cl_2, 1:9). M.p. 66 °C. $[\alpha]_D$ = +3.4 (c = 0.8, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3348, 1757 cm^{-1}. ^1H NMR

(250 MHz, $CDCl_3$): δ = 2.35 (dd, ^2J = 15.3, $J_{2a,1'}$ = 8.5 Hz, 1 H, 2-H_a), 2.62−2.66 (m, 1 H, 6′-H_a), 2.69 (dd, ^2J = 15.3, $J_{2b,1'}$ = 3.8 Hz, 1 H, 2-H_b), 2.83 (s, 2 H, NH_2), 2.99−3.04 (m, 1 H, 6′-H_b), 3.24−3.36 (m, 3 H, 2′-H, 3′-H, 4′-H), 3.57 (s, 3 H, OMe), 3.62−3.74 (m, 2 H, 1′-H, 5′-H), 4.57 (d, ^2J = 11.3 Hz, 1 H, CH-Ph), 4.58 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.79−4.89 (m, 4 H, 4× CH-Ph), 7.19−7.32 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 37.7 (C-2), 43.0 (C-6′), 52.2 (Me), 75.5, 76.0 (OCH_2), 80.0, 81.8, 87.5 (C-1′,2′,3′,4′,5′), 128.1, 128.3, 128.4, 128 .5, 128.9 (CH-Ph), 138.3, 138.7 (C-*ipso*), 171.9 (CO) ppm. $C_{30}H_{35}NO_6$ (505.6): calcd. C 71.27, H 6.98, N 2.77; found C 71.53, H 7.07, N 2.68.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-8,9-didehydro-7,8,9-trideoxy-D-*glycero*-L-*gluco*-nonuronic Acid (9): KBr (20 mg), $NaHCO_3$ (5%, 7.6 mL), TEMPO (275 mg, 1.760 mmol), and NaOCl (4−6%, 2.475 mL) were added at 0 °C to a solution of **6** (767 mg, 1.618 mmol) in acetone (16 mL). After the mixture had been stirred for 1 h at 0 °C, additional NaOCl solution (4−6%, 1.3 mL) was added and the mixture was stirred at room temp. for 20 h. The solution was then concentrated and diluted in EtOAc (50 mL), washed with 10% HCl and brine, dried with $MgSO_4$, filtered, and concentrated to an oil, which was purified by column chromatography (Et_2O/hexane, 1:1 to 2:1) to afford **9** (540 mg, 67%) as an oil. R_f = 0.53 (MeOH/CH_2Cl_2, 1:9). $[\alpha]_D$ = −22.5 (*c* = 0.5, CH_2Cl_2). IR (KBr): ṽ = 3445−2529, 1733 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.18−2.30 (m, 1 H, 7-H_a), 2.48−2.57 (m, 1 H, 7-H_b), 3.26−3.38 (m, 2 H), 3.61−3.73 (m, 2 H), 3.83−3.87 (m, 1 H), 4.56 (d, ^2J = 10.8 Hz, 1 H, CH-Ph), 4.59 (d, ^2J = 10.5 Hz, 1 H, CH-Ph), 4.67−4.98 (m, 4 H, 4× CH-Ph), 5.03−5.06 (m, 2 H, 9-H), 5.71−5.88 (m, 1 H, 8-H), 7.16−7.29 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 36.2 (C-7), 75.5, 75.6, 76.1 (OCH_2), 78.2, 79.6, 80.1, 81.3, 86.7 (C-2,3,4,5,6), 118.1 (C-9), 128.3, 128.4, 128.7, 128.9, 129.0 (CH-Ph), 134.5 (C-8), 137.8, 138.3, 138.6 (C-*ipso*), 174.6 (CO) ppm. $C_{30}H_{32}O_6$ (488.6): calcd. C 73.75, H 6.60; found C 73.90, H 6.49.

Methyl 2,6-Anhydro-3,4,5-tri-*O*-benzyl-8,9-didehydro-7,8,9-trideoxy-D-*glycero*-L-*gluco*-nonuronate (10): Acid **9** (156 mg, 0.320 mmol) was treated with sodium bicarbonate (50 mg, 0.595 mmol) and methyl iodide (50 μL, 0.803 mmol) in DMF to afford ester **10** (142 mg, 88%) as an oil. R_f = 0.73 (Et_2O/hexane, 1:1). $[\alpha]_D$ = −0.4 (*c* = 0.8, CH_2Cl_2), $[\alpha]_D$ = −4 (*c* = 0.5, EtOAc). IR (KBr): ṽ = 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.18−2.30 (m, 1 H, 7-H_a), 2.47−2.56 (m, 1 H, 7-H_b), 3.29−3.32 (m, 2 H), 3.58−3.84 (m, 4 H), 3.65 (s, 3 H, OMe), 4.52 (d, ^2J = 10.8 Hz, 1 H, CH-Ph), 4.57 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.70 (d, ^2J = 10.8 Hz, 1 H, CH-Ph), 4.77−4.87 (m, 3 H, 3× CH-Ph), 4.98−5.05 (m, 2 H, 9-H), 5.72−5.90 (m, 1 H, 8-H), 7.16−7.29 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 36.2 (C-7), 52.9 (OMe), 75.6, 75.7, 76.1 (OCH_2), 78.7, 79.9, 80.7, 81.4, 86.9 (C-2,3,4,5,6), 117.9 (C-9), 128.2, 128.4, 128.5, 129.0 (CH-Ph), 134.7 (C-8), 138.3, 138.5, 138.8 (C-*ipso*), 170.2 (CO) ppm. $C_{31}H_{34}O_6$ (502.6): calcd. C 74.08, H 6.82; found C 74.37, H 6.68.

Methyl 2,6-Anhydro-3,4,5-tri-*O*-benzyl-7-deoxy-D-*glycero*-L-*gluco*-octuronate (11): OsO_4 (4% solution in *t*BuOH, 68 μL) and $NaIO_4$ (107 mg, 0.500 mmol) were added to a solution of compound **10** (125 mg, 0.250 mmol) in a mixture of THF/H_2O (2:1, 0.9 mL). After 20 h of stirring at room temp., the mixture was concentrated, diluted in EtOAc (30 mL), washed with water, 5% $Na_2S_2O_3$, and brine, dried with $MgSO_4$, filtered, and concentrated to a solid, which was dissolved in MeOH (1 mL). $NaBH_4$ (19 mg, 0.500 mmol) was added, and the mixture was stirred for 20 h at room temp. The solution was concentrated, dissolved in EtOAc (30 mL), washed with water, dried with $MgSO_4$, filtered, and concentrated. The residue was purified by preparative layer chromatography (Et_2O/hexane, 1:1) to afford **11** (87 mg, 69%) as an oil. R_f = 0.28 (Et_2O/hexane, 1:1). $[\alpha]_D$ = −13 (*c* = 1, CH_2Cl_2). IR (KBr): ṽ = 3445, 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.73−1.84 (m, 1 H, 7-H_a), 2.08−2.14 (m, 1 H, 7-H_b), 3.33−3.96 (m, 7 H), 3.75 (s, 3 H, OMe), 4.64 (d, ^2J = 10.8 Hz, 1 H, CH-Ph), 4.68 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.76 (d, ^2J = 10.8 Hz, 1 H, CH-Ph), 4.84−4.99 (m, 3 H, 3× CH-Ph), 7.18−7.36 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 34.5 (C-7), 52.9 (OMe), 60.6 (C-8), 75.6, 75.8, 76.1 (OCH_2), 78.5, 79.2, 80.4, 81.6, 86.7 (C-2,3,4,5,6), 128.2, 128.5, 129.0 (CH-Ph), 138.2, 138.7 (C-*ipso*), 170.0 (CO) ppm. $C_{30}H_{34}O_7$ (506.6): calcd. C 71.13, H 6.76; found C 71.28, H 6.61.

Methyl 2,6-Anhydro-8-azido-3,4,5-tri-*O*-benzyl-7,8-dideoxy-D-*glycero*-L-*gluco*-octuronate (2): Alcohol **11** was transformed into azide **2** as for **6**. The crude product was purified by preparative thin-layer chromatography (EtOAc/hexane, 1:5) to afford **2** as a white solid (42 mg, 47%). R_f = 0.73 (EtOAc/hexane, 1:3). M.p. 114−115 °C. $[\alpha]_D$ = −17 (*c* = 1, CH_2Cl_2). IR (KBr): ṽ = 2119, 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.59−1.68 (m, 1 H, 1-H_a), 2.00−2.07 (m, 1 H, 1-H_b), 3.24−3.41 (m, 4 H), 3.61−3.86 (m, 3 H), 3.68 (s, 3 H, OMe), 4.55 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.60 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.74 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.82 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.86 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.89 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 7.18−7.31 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 31.5 (C-7), 48.0 (C-8), 52.9 (OMe), 75.5, 75.8, 76.1 (OCH_2), 77.1, 78.6, 80.6, 81.5, 86.7 (C-2,3,4,5,6), 128.2, 128.4, 128.5, 128.9, 129.0 (CH-Ph), 138.1, 138.6 (C-*ipso*), 170.0 (CO) ppm. $C_{30}H_{33}N_3O_6$ (531.6): calcd. C 67.78, H 6.26, N 7.90; found C 67.90, H 6.24, N 7.99.

3-(6′-*O*-Acetyl-2′,3′,4′-tri-*O*-benzyl-α-D-glucopyranosyl)-1-propene (12):[18] The title compound was prepared as described.[18] Yield: 71%. R_f = 0.50 (Et_2O/hexane, 1:4). M.p. 55 °C. $[\alpha]_D$ = +47 (*c* = 1, CH_2Cl_2). IR (KBr): ṽ = 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.96 (s, 1 H, Ac), 2.37−2.43 (m, 2 H, 3-H), 3.37 (dd, $J_{3',4'}$ = 8.3, $J_{4',5'}$ = 10.0 Hz, 1 H, 4′-H), 3.61 (td, $J_{4',5'}$ = 10.0, $J_{5',6'a}$ = $J_{5',6'b}$ = 3.8 Hz, 1 H, 5′-H), 3.69 (dd, $J_{2',3'}$ = 9.5, $J_{1',2'}$ = 5.5 Hz, 1 H, 2′-H), 3.75 (dd, $J_{2',3'}$ = 9.5, $J_{3',4'}$ = 8.3 Hz, 1 H, 3′-H), 3.97−4.05 (m, 1 H, 1′-H), 4.14−4.15 (m, 2 H, 6′-H_a, 6′-H_b), 4.47 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.54 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.62 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.73 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.78 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.88 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.98−5.06 (m, 2 H, 1-H), 5.60−5.77 (m, 1 H, 2-H), 7.16−7.28 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 21.3 (Me), 30.2 (C-3), 63.9 (C-6′), 70.0 (C-5′), 73.5 (OCH_2), 74.0 (C-1′), 75.5, 75.9 (OCH_2), 78.2 (C-4′), 80.4 (C-2′), 82.7 (C-3′), 117.5 (C-1), 128.2, 128.3, 128.4, 128.6, 128.9 (CH-Ph), 134.7 (C-2), 138.2, 138.5, 138.9 (C-*ipso*), 171.2 (CO) ppm.

3-(2′,3′,4′-Tri-*O*-benzyl-α-D-glucopyranosyl)-1-propene (13):[8c] Compound **12** was treated with MeONa/MeOH to afford pure **13** without purification. Yield: 100%. R_f = 0.20 (EtOAc/hexane, 1:5). M.p. 79 °C. $[\alpha]_D$ = +45.5 (*c* = 1, CH_2Cl_2). IR (KBr): ṽ = 3450 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.75 (t, $J_{OH,6'a}$ = $J_{OH,6'b}$ = 6.8 Hz, 1 H, OH), 2.38−2.44 (m, 2 H, 3-H), 3.42−3.74 (m, 6 H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H_a, 6′-H_b), 3.93−3.99 (m, 1 H, 1′-H), 4.54 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.55 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.64 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.74 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.79 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.86 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.99−5.07 (m, 2 H, 1-H), 5.64−5.75 (m, 1 H, 2-H), 7.17−7.28 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 30.5 (C-3), 62.6 (C-6′), 75.2 (CH), 73.7 (OCH_2), 74.2 (CH), 75.6, 75.9 (OCH_2), 78.6, 80.6, 82.7 (CH), 117.7

(C-1), 128.2, 128.3, 128.4, 128.6, 128.9, 129.0 (CH-Ph), 135.1 (C-2), 138.6, 138.7, 139.2 (C-*ipso*) ppm.

3-(6′-Azido-2′,3′,4′-tri-*O*-benzyl-6′-deoxy-α-D-glucopyranosyl)-1-propene (14):[8c] The alcohol **13** was transformed into **14** as described.[8c] Yield: 75%. R_f = 0.70 (EtOAc/hexane, 1:2). M.p. 55 °C. $[\alpha]_D$ = +64.5 (c = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 2100 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.19 (t, $J_{3a,1'} = J_{3b,1'}$ = 4.8 Hz, 2 H, 3-H), 3.24 (dd, ^2J = 12.8, $J_{5',6'a}$ = 5.3 Hz, 1 H, 6′-H_a), 3.34 (dd, ^2J = 12.8, $J_{5',6'b}$ = 2.3 Hz, 1 H, 6′-H_b), 3.39 (dd, $J_{3',4'}$ = 9.8, $J_{4',5'}$ = 8.3 Hz, 1 H, 4′-H), 3.56−3.65 (m, 1 H, 5′-H), 3.70 (dd, $J_{1',2'}$ = 3.0, $J_{2',3'}$ = 8.3 Hz, 1 H, 2′-H), 3.75 (dd, $J_{2',3'}$ = 8.3, $J_{3',4'}$ = 9.8 Hz, 1 H, 3′-H), 3.76−3.86 (m, 1 H, 1′-H), 4.52 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.57 (d, ^2J = 11.8 Hz, 1 H, CH-Ph), 4.64 (d, ^2J = 11.8 Hz, 1 H, CH-Ph), 4.74 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.83 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.89 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 5.03−5.11 (m, 2 H, 1-H), 5.70−5.81 (m, 1 H, 2-H), 7.17−7.30 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 30.6 (C-3), 52.2 (C-6′), 71.5 (CH), 73.6 (OCH_2), 74.1 (CH), 75.7, 75.9 (OCH_2), 79.3, 80.5, 82.6 (CH), 117.7 (C-1), 128.2, 128.3, 128.4, 128.5, 128.9 (CH-Ph), 134.8 (C-2), 138.4, 138.6, 139.1 (C-*ipso*) ppm.

(6′-Azido-2′,3′,4′-tri-*O*-benzyl-6′-deoxy-α-D-glucopyranosyl)-ethanoic Acid (15):[8c] Compound **14** was oxidized as described.[8c] Purification by column chromatography (EtOAc/hexane 1:3, then MeOH/CH_2Cl_2 1:9) afforded **15** as an oil. Yield: 71%. R_f = 0.50 (EtOAc/hexane, 1:2). $[\alpha]_D$ = +59.3 (c = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 2500−3250, 2175, 1709 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.66 (dd, $J_{1',2a}$ = 9.5, ^2J = 15.3 Hz, 1 H, 2-H_a), 2.77 (dd, $J_{1',2b}$ = 5.3, ^2J = 15.3 Hz, 1 H, 2-H_b), 3.27 (dd, ^2J = 13.0, $J_{5',6'a}$ = 5.0 Hz, 1 H, 6′-H_a), 3.36−3.47 (m, 2 H), 3.64−3.76 (m, 3 H), 4.53 (d, ^2J = 11.3 Hz, 1 H, CH-Ph), 4.58−4.71 (m, 3 H, 1′-H, CH_2-Ph), 4.78 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.86 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.91 (d, ^2J = 11.3 Hz, 1 H, CH-Ph), 7.18−7.38 (m, 15 H, Ph), 10.2 (s, 1 H, CO_2H) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 32.9 (C-2), 51.9 (C-6′), 71.3, 72.1 (CH), 73.4, 75.4, 75.7 (OCH_2), 78.7, 79.4, 82.1 (CH), 128.1, 128.4, 128.9 (CH-Ph), 138.2, 138.4, 138.8 (C-*ipso*) ppm.

Methyl (6′-Azido-2′,3′,4′-tri-*O*-benzyl-6′-deoxy-α-D-pyranosyl)-ethanoate (16):[8c] Compound **15** was esterified as described.[8c] Purification by preparative thin-layer chromatography (EtOAc/cyclohexane, 1:4) afforded **16** as an oil in 46% yield. R_f = 0.74 (EtOAc/cyclohexane, 1:2). $[\alpha]_D$ = +59.2 (c = 1.3, CH_2Cl_2).

Methyl (6′-Amino-2′,3′,4′-tri-*O*-benzyl-6′-deoxy-α-D-glucopyranosyl)ethanoate (3): The azido function of **16** was reduced as for **8**. Purification by preparative thin-layer chromatography (MeOH/CH_2Cl_2, 1:9) afforded **3** as a white solid in 75% yield. R_f = 0.38 (MeOH/CH_2Cl_2, 1:9). M.p. 68 °C. $[\alpha]_D$ = +56.7 (c = 0.3, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3348, 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.07 (s, 2 H, NH_2), 2.64−2.67 (m, 3 H, 2-$H_{a,b}$, 6′-H_a), 2.89−2.94 (m, 1 H, 6′-H_b), 3.25−3.28 (m, 1 H, 4′-H), 3.44−3.50 (m, 1 H, 5′-H), 3.56 (s, 3 H, OMe), 3.63−3.69 (m, 2 H, 2′-H, 3′-H), 4.50−4.62 (m, 4 H, 1′-H, 3× CH-Ph), 4.70 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.74 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.81 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 7.17−7.35 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 32.9 (C-2), 43.2 (C-6′), 52.3 (Me), 71.2 (C-1′), 73.6 (OCH_2), 73.9 (C-5′), 75.3, 75.7 (OCH_2), 79.0 (C-4′), 79.5, 82.0 (C-2′,3′), 128.1, 128.3, 128 .5, 128.9 (CH-Ph), 138.2, 138.3, 138.8 (C-*ipso*), 172.3 (CO) ppm. $C_{30}H_{35}NO_6$ (505.6): calcd. C 71.27, H 6.98, N 2.77; found C 71.47, H 6.92, N 2.69.

Methyl 2,6-Anhydro-3,4,5-tri-*O*-benzyl-8,9-didehydro-7,8,9-trideoxy-L-*gulo*-D-*glycero*-nonanoate (17): Jones reagent (1 M, 3.69 mL, 3.690 mmol) was added to a solution of alcohol **13** (500 mg, 1.055 mmol) in acetone (5 mL). The mixture was stirred for 48 h at room temp. After concentration, the residue was dissolved in EtOAc (50 mL), washed successively with water, $Na_2S_2O_3$ (5%), HCl (5%), and brine, dried with $MgSO_4$, filtered, and concentrated. The corresponding acid was then esterified as for **9**. Purification by column chromatography (Et_2O/cyclohexane, 1:3) afforded **17** (251 mg, 48%) as an oil. R_f = 0.40 (Et_2O/cyclohexane, 1:1). $[\alpha]_D$ = +41.3 (c = 0.4, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ = 2.33−2.52 (m, 2 H, 7-H), 3.48 (dd, $J_{5,6}$ = 4.0, $J_{4,5}$ = 6.3 Hz, 1 H, 5-H), 3.62 (s, 3 H, OMe), 3.73 (dd, $J_{4,5}$ = 6.3, $J_{3,4}$ = 5.8 Hz, 1 H, 4-H), 3.87 (t, $J_{3,4} = J_{2,3}$ = 5.8 Hz, 1 H, 3-H), 4.14−4.21 (m, 1 H, 1-H), 4.32 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 4.42−4.66 (m, 6 H, 3× OCH_2), 4.97−5.13 (m, 2 H, 9-H), 5.70−5.82 (m, 1 H, 8-H), 7.16−7.32 (m, 15 H, Ph) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 32.8 (C-7), 52.4 (OMe), 72.6 (C-6), 72.8 (OCH_2), 73.0 (C-2), 73.7, 73.8 (OCH_2), 76.2 (C-4), 76.4 (C-3), 76.6 (C-5), 117.4 (C-9), 127.8, 128.0, 128.2, 128.3, 128.6 (Ph), 134.5 (C-8), 138.0, 138.1 (C-*ipso*), 170.6 (CO) ppm. $C_{31}H_{34}O_6$ (502.6): calcd. C 74.08, H 6.82; found C 74.35, H 6.70.

Methyl 2,6-Anhydro-3,4,5-tri-*O*-benzyl-7-deoxy-D-*glycero*-L-*gluco*-octuronate (18): Compound **17** was transformed into **18** as for compound **10**. Purification by column chromatography (Et_2O/cyclohexane, 1:1 to 2:1) afforded the title compound as an oil in 30% yield. R_f = 0.72 (Et_2O). $[\alpha]_D$ = +37.6 (c = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3445, 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ = 1.50−1.57 (m, 1 H, 7-H_a), 2.02−2.12 (m, 1 H, 7-H_b), 2.85 (s, 1 H, OH), 3.23−3.26 (m, 1 H, 5-H), 3.57 (s, 3 H, OMe), 3.67 (t, $J_{4,5} = J_{3,4}$ = 4.3 Hz, 1 H, 4-H), 3.68−3.89 (m, 2 H, 8-H), 3.93 (t, $J_{2,3} = J_{3,4}$ = 3.3 Hz, 1 H, 3-H), 4.26 (td, J = 2.8, 11.0 Hz, 1 H, 6-H), 4.30 (d, ^2J = 11.8 Hz, 1 H, CH-Ph), 4.38 (d, ^2J = 11.8 Hz, 1 H, CH-Ph), 4.40 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.45 (d, $J_{2,3}$ = 3.0 Hz, 1 H, 2-H), 4.52 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.60 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.65 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 7.06−7.29 (m, 15 H, Ph) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 32.3 (C-7), 52.7 (OMe), 59.9 (C-8), 69.5 (C-6), 72.8 (OCH_2), 73.2 (C-4), 73.1 (OCH_2), 74.2 (C-2), 74.4 (C-3), 75.7 (C-5), 127.9, 128.3, 128.5, 128.7, 128.8, 128.9 (Ph), 138.0, 138.3 (C-*ipso*), 171.4 (CO) ppm. $C_{30}H_{34}O_7$ (518.6): cald. C 71.13, H 6.76; found C 71.00, H 6.82.

Methyl 2,6-Anhydro-8-azido-3,4,5-tri-*O*-benzyl-7,8-dideoxy-D-*glycero*-L-*gluco*-octuronate (4): Alcohol **18** was transformed into azide **4** as for **6**. The crude product was purified by preparative thin-layer chromatography (EtOAc/hexane, 1:5) to afford **4** as an oil in 69% yield. R_f = 0.66 (Et_2O/cyclohexane, 3:2). $[\alpha]_D$ = +35 (c = 0.4, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 2119, 1757 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.58−1.62 (m, 1 H, 7-H_a), 2.05−2.20 (m, 1 H, 7-H_b), 3.36−3.39 (m, 1 H, 5-H), 3.42−3.47 (m, 2 H, 8-H), 3.66 (s, 3 H, OMe), 3.73 (t, $J_{4,5} = J_{3,4}$ = 5.0 Hz, 1 H, 4-H), 3.98 (dd, $J_{3,4}$ = 5.0, $J_{2,3}$ = 4.5 Hz, 1 H, 3-H), 4.22−4.27 (m, 1 H, 6-H), 4.43 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.44 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.46 (d, $J_{3,4}$ = 4.5 Hz, 1 H, 2-H), 4.53 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.61 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.67 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.69 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 7.17−7.37 (m, 15 H, Ph) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 29.1 (C-7), 48.5 (C-8), 52.6 (OMe), 69.8 (C-6), 72.8, 73.3, 73.6 (OCH_2), 73.8 (C-2), 74.2 (C-4), 75.3 (C-3), 76.0 (C-5), 128.1, 128.3, 128.5, 128.7, 128.9 (CH-Ph), 138.2 (C-*ipso*), 170.8 (CO) ppm. $C_{30}H_{33}N_3O_6$ (531.6): cald. C 67.78, H 6.26, N 7.90; found C 67.60, H 6.34, N 8.03.

Saccharide Nucleoside 20: IIDQ (50 μL, 0.168 mmol) was added to a solution of acid **9** (55 mg, 0.113 mmol) and 5′-amino-2′,3′-di-*O*-benzyl-5′-deoxyuridine **19**[19] (47 mg, 0.111 mmol) in anhydrous CH_2Cl_2. The solution was stirred for 20 h at room temp., and then purified by preparative thin-layer chromatography (Et_2O/hexane,

3:1) to afford **20** as a white solid (55 mg, 69%). R_f = 0.55 (MeOH/CH_2Cl_2, 1:19). M.p. 70 °C. $[\alpha]_D$ = +3.4 (*c* = 0.7, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3348, 1709, 1685 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.27−2.33 (m, 1 H), 2.56−2.61 (m, 1 H), 3.36−3.87 (m, 8 H), 4.19−4.28 (m, 2 H), 4.48 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.57 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.58 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.64 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.71 (d, ^2J = 12.0 Hz, 1 H, CH-Ph), 4.74−4.96 (m, 5 H, 5 × CH-Ph), 5.04−5.11 (m, 2 H, CH_2=), 5.65−5.70 (m, 2 H), 5.76−5.92 (m, 1 H, CH=), 6.79 (t, *J* = 5.6 Hz, 1 H, NH), 7.14 (d, *J* = 8.3 Hz, 1 H, CH=), 7.24−7.35 (m, 25 H, Ph), 9.56 (s, 1 H, NH) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 36.3 (CH_2), 41.3 (CH_2-N), 72.8, 73.1, 75.2, 75.3, 75.8 (OCH_2), 78.6, 78.8, 79.0, 80.5, 81.0, 81.4, 86.2, 92.2 (CH), 102.9 (CH_2=), 118.0 (CH=), 128.2, 128.4, 128.6, 128.7, 128.8, 129.0 (CH-Ph), 134.5 (CH=), 137.6, 138.4, 138.7 (C-*ipso*), 141.5 (CH=), 150.3, 163.8, 169.9 (CO) ppm. $C_{53}H_{55}N_3O_{10}$ (896.1): cald. C 71.20, H 6.20, N 4.70; found C 71.25, H 6.30, N 4.78.

Disaccharide Nucleoside 23: The olefin function in compound **20** was oxidized as for **7** to give the acid **21** (yield: 100%), which was used without purification. *i*BuOCOCl (2.8 μL, 0.022 mmol) and TEA (3 μL, 0.022 mmol) were added at −10 °C, under argon, to a solution of acid **21** (18 mg, 0.020 mmol) in anhydrous CH_2Cl_2. After the mixture had been stirred for 10 min, a solution of 2-(2′-acetylamino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-α-D-glucopyranosyl)-ethylamine (**22**)[20] (10 mg, 0.020 mmol) in anhydrous CH_2Cl_2 (0.5 mL) was added. The mixture was stirred for 20 h at room temp., and was then diluted in EtOAc (20 mL). The organic solution was washed with water, dried with $MgSO_4$, filtered, concentrated, and purified by preparative thin-layer chromatography (EtOAc) to afford **23** as a white solid (16 mg, 69%). R_f = 0.55 (MeOH/CH_2Cl_2, 1:19). M.p. 210 °C. $[\alpha]_D$ = −17.3 (*c* = 1.2, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3325, 1709, 1685 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.43−1.60 (m, 2 H, CH_2), 1.82 (s, 3 H, Ac), 2.17 (dd, ^2J = 15.0, ^3J = 8.5 Hz, 1 H), 2.55 (dd, ^2J = 15.0, ^3J = 3.0 Hz, 1 H), 3.07−3.16 (m, 2 H, CH_2-N), 3.26−3.45 (m, 6 H), 3.61−3.99 (m, 6 H), 4.05−4.08 (m, 2 H), 4.16−4.19 (m, 2 H), 4.30 (dd, *J* = 4.1, 4.7 Hz, 1 H), 4.38−4.53 (m, 10 H), 4.58 (d, ^2J = 11.5 Hz, 1 H, CH-Ph), 4.63 (d, ^2J = 11.8 Hz, 1 H, CH-Ph), 4.75−4.91 (m, 4 H), 5.41 (d, *J* = 4.5 Hz, 1 H), 5.56 (d, *J* = 8.0 Hz, 1 H, CH=), 6.49 (d, *J* = 8.5 Hz, 1 H, NH), 6.85 (m, 1 H, NH), 7.02 (d, *J* = 8.0 Hz, 1 H, CH=), 7.19−7.31 (m, 41 H, NH, Ph), 9.50 (s, 1 H, NH) ppm. ^{13}C (62.9 MHz, $CDCl_3$): δ = 23.7 (Ac), 30.1, 37.6, 39.5, 40.8 (CH_2), 49.0 (CH-N), 67.3 (OCH_2), 68.1 (CH), 72.7, 72.8, 73.1, 73.2, 73.5 (OCH_2), 74.1, 74.5, 74.9 (CH), 75.1, 75.2, 75.8 (OCH_2), 76.5, 78.2, 78.9, 80.0, 81.2, 81.7, 86.4, 94.0 (CH), 102.9 (CH=), 128.2, 128.4, 128.7, 128.8, 128.9, 129.0 (CH-Ph), 137.8, 138.0, 128.3, 138.7 (C-*ipso*), 142.7 (CH=), 150.5, 163.4, 169.4, 170.5, 170.7 (CO) ppm. FAB-MS: *m*/*z* (%) = 1412.6 (13) [M^+ + 1]. $C_{83}H_{89}N_5O_{16}$ (1412.6): calcd. C 70.57, H 6.35, N 4.96; found C 70.33, H 6.40, N 4.81.

Saccharide Nucleoside 24: 1,3-Diisopropylcarbodiimide (32 μL, 0.200 mmol) and a solution of HOBt (27 mg, 0.200 mmol) in anhydrous THF (0.5 mL) were added at 0 °C to a solution of acid **15** (104 mg, 0.200 mmol) and amine **19** (84 mg, 0.200 mmol) in anhydrous CH_2Cl_2 (2 mL). The solution was stirred at room temp. for 22 h. After concentration in vacuo, the residue was dissolved in EtOAc (20 mL), washed successively with water and brine, dried with $MgSO_4$, filtered, concentrated, and purified by preparative layer chromatography (MeOH/CH_2Cl_2, 1:15) to afford **24** as a white solid (98 mg, 53%). R_f = 0.60 (MeOH/CH_2Cl_2, 1:19). M.p. 92 °C. $[\alpha]_D$ = +22.2 (*c* = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3348, 2119, 1709 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.51 (d, *J* = 6.8 Hz, 2 H, CH_2-CO), 3.15 (dd, *J* = 6.3, ^2J = 10.0 Hz, 1 H, CH-N_3), 3.26−3.33 (m, 3 H), 3.51−3.64 (m, 4 H), 3.81 (t, *J* = 5.5 Hz, 1 H), 4.10−4.16 (m, 1 H), 4.22 (t, *J* = 5.0 Hz, 1 H), 4.39−4.54 (m, 7 H), 4.63 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 4.64 (d, ^2J = 11.3 Hz, 1 H, CH-Ph), 4.75 (d, ^2J = 11.3 Hz, 1 H, CH-Ph), 4.79 (d, ^2J = 11.0 Hz, 1 H, CH-Ph), 5.40 (d, *J* = 4.0 Hz, 1 H), 5.50 (d, ^2J = 8.0 Hz, 1 H, CH=), 6.69 (t, *J* = 3.8 Hz, 1 H, NH), 6.92 (d, ^2J = 8.0 Hz, 1 H, CH=), 7.14−7.33 (m, 25 H, Ph), 8.82 (s, 1 H, NH). ^{13}C (62.9 MHz, $CDCl_3$): δ = 34.2, 41.4, 52.2 (CH_2), 71.4, 72.2 (CH), 73.1, 73.4, 75.3, 75.4 (OCH_2), 77.5, 78.5, 78.6, 79.3, 81.3, 81.8, 93.7 (CH), 102.9 (CH=), 128.3, 128.5, 128.7, 128.9, 129.0 (CH-Ph), 137.6, 137.7, 138.0, 138.1, 138.6 (C-*ipso*), 142.5 (CH=), 150.4, 163.5, 171.1 (CO) ppm. $C_{52}H_{54}N_6O_{10}$ (923.0): calcd. C 67.67, H 5.90, N 9.10; found C 67.93, H 5.84, N 9.24.

Saccharide Nucleoside 25: Azide **24** was reduced to amine **25** as for **8**. Column purification (MeOH/CH_2Cl_2, 1:19 to 1:9) afforded amine **25** as a white solid in 86% yield. R_f = 0.35 (MeOH/CH_2Cl_2, 1:9). M.p. 208 °C. $[\alpha]_D$ = +36.8 (*c* = 0.8, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3373, 3300, 1709, 1685 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.65−2.79 (m, 3 H), 3.05−3.09 (m, 1 H), 3.20−3.27 (m, 1 H), 3.36−3.50 (m, 1 H), 3.65−3.91 (m, 5 H), 4.11−4.15 (m, 1 H), 4.22−4.30 (m, 3 H, CH + NH_2), 4.44−4.91 (m, 11 H, CH + 5× CH_2-Ph), 5.63 (d, ^2J = 8.0 Hz, 1 H, CH=), 5.80 (d, *J* = 3.8 Hz, 1 H), 7.09 (d, ^2J = 8.0 Hz, 1 H, CH=), 7.16−7.32 (m, 26 H, NH + Ph), 8.59 (s, 1 H, NH). ^{13}C (62.9 MHz, $CDCl_3$): δ = 33.6, 41.8, 42.8 (CH_2), 71.9, 72.4 (CH), 72.8, 73.2, 75.1, 75.5 (OCH_2), 78.8, 79.3, 79.4, 81.5, 81.7, 91.5 (CH), 103.4 (CH=), 128.3, 128.4, 128.7, 128.9, 129.0, 130.1 (CH-Ph), 137.5, 137.6, 138.2, 138.8 (C-*ipso*), 140.8 (CH=), 151.2, 164.3, 172.0 (CO) ppm. $C_{52}H_{56}N_4O_{10}$ (897.0): Cald. C 69.63, H 6.29, N 6.25; found C 69.90, H 6.19, N 6.22.

(2′-*N*-Acetylamino-3′,4′,5′-tri-*O*-benzyl-2′-deoxy-α-D-glucopyranosyl)ethanoic Acid (27): (2′-Acetylamino-3′,4′,5′-tri-*O*-benzyl-2′-deoxy-α-D-glucopyranosyl)-1-propene (**26**)[19] was oxidized as described for **7**. The crude product was used without purification. Yield: 69%. R_f = 0.22 (MeOH/CH_2Cl_2, 1:9). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.82 (s, 3 H, Ac), 2.30 (m, 2 H, 2-H), 3.38−3.55 (m, 5 H), 4.18−4.22 (m, 2 H), 4.36−4.63 (m, 6 H, 3 × CH_2-Ph), 6.85 (d, $J_{NH,2'}$ = 9.0 Hz, 1 H, NH), 7.20−7.29 (m, 15 H, Ph) ppm.

Disaccharide Nucleoside 28: *i*BuOCOCl (3 μL, 0.023 mmol) and TEA (3.2 μL, 0.023 mmol) were added at −10 °C, under argon, to a solution of acid **27** (11 mg, 0.021 mmol) in anhydrous CH_2Cl_2 (0.5 mL). After the mixture had been stirred for 10 min, a solution of amine **25** (19 mg, 0.021 mmol) in anhydrous CH_2Cl_2 (0.5 mL) was added. The mixture was stirred for 20 h at room temp., and was then diluted in EtOAc (20 mL). The organic solution was washed with water, dried with $MgSO_4$, filtered, concentrated, and purified by preparative layer chromatography (EtOAc/cyclohexane, 5:2) to afford **28** as a white solid (17 mg, 56%). R_f = 0.66 (EtOAc). M.p. 192 °C. $[\alpha]_D$ = +5.9 (*c* = 1.8, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3325, 1709, 1685 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.70 (s, 3 H, Ac), 2.11−2.57 (m, 4 H, 2 × CH_2), 3.17−3.89 (m, 14 H), 4.10−4.71 (m, 21 H), 5.35 (d, *J* = 4.3 Hz, 1 H), 5.49 (d, ^2J = 8.0 Hz, 1 H, CH=), 6.73 (m, 3 H, 3 × NH), 6.90 (d, ^2J = 8.0 Hz, 1 H, CH=), 7.13−7.50 (m, 40 H, Ph), 9.14 (s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.7 (Ac), 30.1, 39.4, 40.7, 41.1 (CH_2), 48.3, 66.0 (CH), 68.0 (CH_2), 70.9, 71.6 (CH), 72.3, 72.4, 73.0, 73.2, 73.6, 74.2, 75.1, 75.3 (OCH_2), 77.5, 78.5, 78.8, 79.3, 81.2, 81.9, 94.3 (CH), 103.0 (CH=), 128.1, 128.3, 128.4, 128.9, 130.2 (Ph), 137.6, 137.7, 138.2, 138.3, 138.5, 138.7 (C-*ipso*), 142.9 (CH=), 150.4, 163.3, 170.5, 171.1, 171.5 (CO) ppm. FAB-MS: *m*/*z* (%) = 1412.7 (22) [M^+ + 1]. $C_{83}H_{89}N_5O_{16}$ (1412.6): calcd. C 70.57, H 6.35, N 4.96; found C 70.77, H 6.43, N 4.89.

Disaccharide Nucleoside 29: A solution of **28** (65 mg, 0.046 mmol) in MeOH (1 mL) was hydrogenated at atmospheric pressure in the presence of 10% palladium on charcoal (18 mg) for 15 h at room temp. The catalyst was filtered off and the filtrate was concentrated to give 23 mg (72%) of the title compound as a white solid. M.p. 220−222 °C. ^{1}H NMR (250 MHz, D_2O): δ = 2.02 (s, 3 H, Ac), 2.51−2.72 (m, 4 H, 2× CH_2), 3.23 (t, J = 9.5 Hz, 1 H), 3.36−3.76 (m, 13 H), 3.99 (dd, J = 5.8, 10.8 Hz, 1 H), 4.05−4.15 (m, 1 H), 4.16 (t, J = 5.8 Hz, 1 H), 4.39−4.57 (m, 2 H), 5.75 (d, J = 4.3 Hz, 1 H), 5.87 (d, ^2J = 8.0 Hz, 1 H, CH=), 7.65 (d, ^2J = 8.0 Hz, 1 H, CH=) ppm. FAB-MS: *m*/*z* (%) = 714.2 (4) $[M + Na]^+$, 692.2 (12) $[M^+ + 1]$.

Trisaccharide Nucleoside 31: A solution of $ZnCl_2$ (1.4 mg, 0.010 mmol) and $NaBH_3CN$ (1.2 mg, 0.020 mmol) in MeOH (0.5 mL) was added to a solution of the amine **25** (9 mg, 0.010 mmol) and (2′-acetylamino-3′,4′,5′-tri-*O*-benzyl-2′-deoxy-α-D-glucopyranosyl)ethanal (**30**)[19] (10 mg, 0.020 mmol) in MeOH (0.5 mL). After 20 h of stirring at room temp., NaOH (0.1 N, 0.2 mL) was added. The solution was concentrated in vacuo. The residue was dissolved in EtOAc, washed with water and brine, dried with $MgSO_4$, filtered, concentrated, and purified by preparative layer chromatography (CH_2Cl_2/MeOH, 15:1) to afford **31** as a white solid (7 mg, 37%). R_f = 0.23 (EtOAc). M.p. 78 °C. $[\alpha]_D$ = +15.8 (c = 0.4, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.70 (s, 6 H, 2 × Ac), 1.71−1.97 (m, 4 H, 2 × CH_2), 2.40−2.65 (m, 6 H), 3.02−3.08 (m, 1 H), 3.37−3.67 (m, 16 H), 4.02−4.33 (m, 8 H), 4.37−4.75 (m, 22 H), 5.48 (d, J = 4.3 Hz, 1 H), 5.48 (d, ^2J = 7.8 Hz, 1 H, CH=), 5.64 (d, J = 2.8 Hz, 1 H), 6.50 (m, 1 H, NH), 6.67 (d, J = 9.3 Hz, 2 H, 2 × NH), 7.07−7.26 (m, 56 H, CH= + Ph), 7.96 (s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.6 (Ac), 28.3, 30.1, 33.2, 40.7 (CH_2), 48.7 (CH), 51.6, 56.3 (CH_2), 67.6 (CH), 68.5 (CH_2), 71.0, 71.5 (CH), 72.5, 72.7, 73.0, 73.5 (OCH_2), 73.9, 75.1 (CH), 75.4 (OCH_2), 77.2, 78.8, 79.3, 80.0, 82.1, 91.4 (CH), 102.3 (CH=), 128.1, 128.3, 128.4, 128.8, 128.9 (Ph), 137.8, 138.1, 138.3, 138.6 (C-*ipso*), 141.6 (CH=), 150.4, 163.4, 170.4, 170.5, 172.2 (CO) ppm. FAB-MS: *m*/*z* (%) = 1899.9 (28) $[M^+ + 1]$. $C_{114}H_{126}N_6O_{20}$ (1900.3): calcd. C 72.06, H 6.68, N 4.42; found C 72.32, H 6.76, N 4.33.

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